

**REMARKS/ARGUMENTS**

Status of the Claims

Claims 2-4 and 25-46 were rejected. Claims 2, 32, and 42 have been amended. Claims 37-41 have been canceled without prejudice or disclaimer. Claims 2-4, 25-36 and 42-46 are pending.

Claim 2 has been amended to clarify that the claimed isolated nucleic acid molecule comprises a nucleotide sequence having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 3, wherein said sequence encodes a polypeptide having LOX activity. Support for the amendment to claim 2 can be found throughout the specification, particularly on page 14, lines 23-28, and page 15, lines 22-25.

Claim 32 has been amended to independent form. As amended, claim 32 no longer depends from claim 2. The amendment of claim 32 is fully supported by the specification.

Claim 42 has been amended to clarify that the claimed isolated nucleic acid molecule comprises a nucleotide sequence having at least 200 contiguous nucleotides of SEQ ID NO: 3, wherein said sequence encodes a full-length LOX polypeptide having LOX activity. The term "sequence" has also been inserted immediately following the term "nucleotide" in the claim. The term "sequence" had been inadvertently omitted from the first presentation of claim 42. In addition, claim 42 has been amended to more distinctly point out that the isolated nucleic acid molecule encodes a full-length LOX polypeptide having LOX activity. Support for the amendment to claim 42 can be found throughout the specification, particularly on: page 12, lines 30-31; page 13, lines 1-9 and 15-19; page 14, lines 15-32; and pages 15-17.

No new matter has been added by way of the amendments to the claims.

Reexamination and reconsideration of the application as amended are respectfully requested in view of the following remarks.

The Objection to the Specification Should Be Withdrawn

The title was objected to for not being descriptive. The title has been amended to recite "SUNFLOWER LOX POLYNUCLEOTIDES AND RELATED COMPOSITIONS". The amendment to the title is not intended to limit the scope of Applicants' claimed invention to LOX polynucleotides that are isolatable from sunflower. Applicants amended the title solely for the purpose of placing the application in a form ready for allowance. Applicants submit that the amended title is sufficiently indicative of the claimed invention and that the objection to the title should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. §112, First Paragraph, Should Be Withdrawn

*Written Description*

Claims 2-4, 25-26, and 32-46 remain rejected under 35 U.S.C. §112, first paragraph, for lack of sufficient written description. Claims 37-41 have been canceled. Claims 2, 32, and 42 have been amended. This rejection is respectfully traversed.

The Examiner maintains that the recitation of 90% sequence identity to SEQ ID NO: 3, hybridization to SEQ ID NO: 3, and a fragment comprising at least 200 contiguous nucleotides of SEQ ID NO: 3 does not describe structural elements that are common among and unique to the claimed genus of nucleic acid molecules. The Office Action indicates that the claims 32-36 have been included in this rejection because Applicant has not met the deposit requirement.

While Applicants continue to maintain, the written description requirement has been satisfied as it relates to claims 2-4, 25-26 and 32-46, to expedite prosecution, claims 37-41 have been canceled, and claim 32 has been rewritten to independent form. Thus, following this amendment to claim 32, claims 32-36 do not recite the percent sequence identity limitation. In addition, as discussed more fully below in the section titled "*Enablement*", Applicants submit concurrently herewith a new declaration stating that the criteria for the deposit have been met. The new declaration includes the change in wording as suggested by the Examiner in the Office

Action. Thus, claims 32-36 satisfy written description requirement of 35 U.S.C. §112, first paragraph.

Additionally, Applicants have amended claims 2 and 46. Amended claim 2 recites that the nucleotide sequence shares at least 95% sequence identity to the sequence of SEQ ID NO: 3 and that the nucleotide sequence encodes a polypeptide having LOX activity. Amended claim 42 recites that the nucleotide sequence has at least 200 contiguous nucleotides of SEQ ID NO: 3 and encodes a full-length LOX polypeptide having LOX activity.

The recitation of at least 95% sequence identity, as recited in claims 2-4 and 25-26, is a very predictable structure of the sequences encompassed by the claimed invention. Moreover, the claims recite the GAP algorithm to be used to determine the percent sequence identity. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (January 5, 2001). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, a sequence having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 3.

Similarly, the recitation of nucleotide sequence having at least 200 contiguous nucleotides of SEQ ID NO: 3, as recited in claims 42-46, is a very predictable structure of the sequences encompassed by the claimed invention. Moreover, these claims recite that the nucleotide sequence encodes a full-length LOX polypeptide. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. at 1106. Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention,

*i.e.*, a nucleotide sequence having at least 200 contiguous nucleotides of SEQ ID NO: 3 and encoding a full-length LOX polypeptide.

The Examiner is again reminded that the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 U.S.P.Q.2d 1662, 1669 (Bd. Pat. App. & Int. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs, defined by a nucleotide sequence, falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also*, Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. at 1106. The recitation in claims 2-4 and 25-26 of a predictable structure of at least 95% sequence identity to SEQ ID NO: 3 is sufficient to satisfy the written description requirement. Similarly, the recitation in claims 42-46 of a predictable structure of at least 200 contiguous nucleotides of SEQ ID NO: 3, wherein the nucleotide sequence encodes a full-length LOX polypeptide, is also sufficient to satisfy the written description requirement.

Moreover, an Applicant may rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. *Id.*, *citing Lilly* at 1568. Claims 2 and 42 have been amended to replace "LOX-like activity" with "LOX activity". Thus, claims 2-4, 25-26 and 42-46 recite that the claimed sequences encode a polypeptide having LOX activity, thereby providing a functional characterization of the sequences claimed in each genus.

In the Amendment and Response filed on October 23, 2003 and the Amendment After Final filed on March 17, 2003, Applicants requested the Examiner to consider Example 14 of the Synopsis of Application of Written Description Guidelines. Again, Applicants submit that claims 2-4, 25-26, and 42-46 parallel this example. The Examiner is requested to reconsider the Example 14 in view of the amended claims that now recite a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 3, or a nucleotide sequence having at least 200

contiguous nucleotides of SEQ ID NO: 3, wherein sequence encodes a full-length LOX polypeptide. As in Example 14, the specification discloses the nucleic acid sequence of SEQ ID NO: 3, and the amended claims recite a limitation requiring the compound to have a specific function, LOX activity.

Consequently, contrary to the Examiner's conclusion, the sequences encompassed by the genus of claims 2-4, 25-26, and 42-46 are defined by relevant identifying physical and chemical properties. In fact, the common attributes or features of the elements possessed by the members of the genus is that they: (1) encode a polypeptide having LOX activity, and (2) either share at least 95% sequence identity at the nucleotide level to the disclosed nucleotide sequence of SEQ ID NO: 3, or have at least 200 contiguous nucleotides of SEQ ID NO: 3, wherein said sequence encodes a full-length LOX polypeptide. The written description requirement of 35 U.S.C. §112, first paragraph, has been satisfied.

In summary, in view of the arguments above, claims 2-4, 25-36 and 42-46 and satisfy the written description requirement of 35 U.S.C. §112, first paragraph, and the Examiner is respectfully requested to withdraw the rejection.

#### *Enablement*

Claims 32-36 were rejected under 35 U.S.C. §112, first paragraph, for not satisfying the requirements of 37 C.F.R. 1.808 related to the deposit of biological material. Applicants submit currently herewith a new declaration that is sufficient to satisfy the deposit requirement under 37 C.F.R. 1.808. This rejection is respectfully traversed.

The Examiner states that the declaration filed on July 23, 2002 is not sufficient to satisfy the deposit requirement under 37 C.F.R. 1.808 because the declaration of June 23, 2003 incorrectly recites the conjunction "or" in section 5(b). The Examiner has indicated that the deposit requirement can be satisfied by resubmitting a declaration in which the aforementioned "or" has been replaced with "and". Applicants submit concurrently herewith a declaration that was been modified as the Examiner has suggested. Accordingly, the Examiner is respectfully

requested to withdraw the rejection of claims 32-36 under 35 U.S.C. §112, first paragraph, for lack of enablement.

Claims 2-4 and 25-46 remain rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. Claims 37-41 have been canceled. Claims 2, 32, and 42 have been amended. This rejection is respectfully traversed.

In the Office Action, the Examiner acknowledges that the specification is enabling for claims limited to a nucleic acid molecule of SEQ ID NO: 3 or a deposit thereof as Accession No. PTA-287 and that encodes a polypeptide having LOX activity, a DNA construct comprising said nucleic acid molecule operably linked to a promoter, and a transformed host cell comprising said DNA construct.

Claims 27 and dependent claims 28-31 were included in the rejection. Claim 27 is drawn to an isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of a nucleic acid molecule comprising a nucleotide sequence set forth in SEQ ID NO: 3, a nucleic acid molecule comprising a nucleotide sequence encoding an amino acid sequence set forth in SEQ ID NO: 4, and a nucleic acid molecule comprising an antisense nucleotide sequence of SEQ ID NO: 3. Dependent claims 28-31 are drawn to DNA constructs, cells, and vectors, which comprises the nucleic acid molecule of claim 27.

In the Office Action mailed January 15, 2003, the Examiner indicated that the claims are enabling for a sunflower nucleic acid molecule of SEQ ID NO: 3, a DNA construct comprising SEQ ID NO: 3, and a transformed host cell comprising SEQ ID NO: 3. Accordingly, in the Amendment After Final dated March 17, 2003, Applicants amended claim 27 to independent form. However, the Examiner has maintained the rejection of claims 27-31.

In contrast to the view of the Office Action, Applicants submit that claims 27-31 are fully enabled. Applicants have provided the sequences of SEQ ID NO: 3 and SEQ ID NO: 4. Furthermore, in view of the disclosure of SEQ ID NO: 3, one of ordinary skill in the art would be able to make and/or use the antisense sequence corresponding to SEQ ID NO: 3. Finally, while those of ordinary skill in the relevant art would be quite familiar with any number of methods for

assaying LOX activity, the specification provides sufficient guidance for assaying LOX enzymatic activity on page 14 at lines 22-25. Accordingly, independent claim 27 and dependent claims 28-31 satisfy the enablement requirements of 35 U.S.C. §112, first paragraph, and the Examiner is respectfully requested to withdraw the rejection and allow these claims.

In the Office Action, the Examiner indicates that Applicants broadly claim an isolated nucleic acid having 90% sequence identity to SEQ ID NO: 3, or that hybridizes under stringent conditions to SEQ ID NO: 3, wherein said nucleic acid molecule encodes a polypeptide having LOX-like activity, or that comprises at least 200 consecutive nucleotides of SEQ ID NO: 3, wherein said nucleic acid molecule encodes a polypeptide having LOX-like activity. The Examiner asserts that Applicant neither teaches the enzymatic activity of the protein encoded by SEQ ID NO: 3 nor how to use the nucleic acid of SEQ ID NO: 3.

In contrast to the view of the Examiner, the specification discloses that SEQ ID NO: 3 encodes a lipoxxygenase and teaches that lipoxxygenase activity can be assayed by any method known in the art including the methods cited in the specification. *See*, for example, pages 2 (lines 19-21), 3 (lines 25-28), 6 (lines 6-8), and 15 (lines 14-25).

The Examiner continues to maintain that a sequence having 90% sequence identity to SEQ ID NO: 3 and a sequence having at least 200 contiguous nucleotides of SEQ ID NO: 3 are not enabled. While Applicants maintain that claims drawn to nucleotide sequences having at least 90% sequence identity, having at least 200 contiguous nucleotides of SEQ ID NO: 3, or that hybridize to the complement of SEQ ID NO: 3 under specified conditions are enabled, Applicants, to expedite prosecution, have amended claims 2, 32, and 42 and have canceled claims 37-41. Applicants, however, expressly reserve the right to file one or more continuing applications drawn to the subject matter of the cancelled claims.

First, Applicants have amended claim 32 to independent form. As amended, this claim no longer recites the percent sequence identity limitation of claim 2. Accordingly, in view of the amendment to claim 32 and the new declaration discussed above, claims 32-36 satisfy the enablement requirement under 35 U.S.C. §112, first paragraph.

Second, Applicants have amended claims 2 and claim 42 to read as follows. Amended claim 2 recites that the isolated nucleic acid molecule comprises a nucleotide sequence having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 3, wherein said sequence encodes a polypeptide having LOX activity and wherein said sequence identity to SEQ ID NO: 3 is determined using the GAP algorithm using default parameters. Amended claim 42 recites an isolated nucleic acid molecule comprising a nucleotide sequence having at least 200 contiguous nucleotides of SEQ ID NO: 3, wherein said sequence encodes a full-length LOX polypeptide having LOX activity.

As made of record in the Amendment and Response filed on October 23, 2002 and the Amendment After Final filed March 17, 2003, Applicants have provided the exemplary nucleotide sequences of SEQ ID NO: 3 and the exemplary polypeptide sequences of SEQ ID NO: 4. The sequences of the invention in claims 2-4 and 25-26 vary from these exemplary sequences by structural parameters (*i.e.*, 95% percent sequence identity to SEQ ID NO: 3). Moreover, these claims explicitly recite the GAP algorithm to be used to determine the percent sequence identity. Similarly, the nucleotide sequences of claims 42-46 have at least 200 contiguous nucleotides of SEQ ID NO: 3 and encode a full-length LOX polypeptide. Furthermore, the claimed sequences are required to retain LOX functionality. The specification provides guidance regarding methods for assaying the desired LOX activity (*i.e.*, LOX enzymatic activity). *See*, for example, page 15, lines 14-25 that provides routine assays for LOX activity. Thus, one of skill in the art would readily be able to make a sequence encompassed by the claims and determine its functionality in a routine assay.

As Applicants stated in the previous two responses, the appropriate standard for determining whether undue experimentation would be required to make and use an invention is discussed in *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) and *In re Jackson*, 217 U.S.P.Q. 804, 807 (Bd. Pat. App. & Int. 1982). *In re Wands* sets forth the "Wands factors," which are used by courts to assess whether experimentation is "undue." Thus, the applicability of *In re Wands* is not limited to experiments with antibodies but rather is relevant to a wide variety of molecular biology experiments. Applicants emphasize that it is now customary in the art to



make a number of sequences and to test them in a large-scale assay for a desired function and that therefore, such experimentation is not "undue." For example, routine experiments involve what is commonly referred to as "shuffling," as described for example in U.S. Patent No. 5,837,458, issued November 17, 1998 with inventors Minshull and Stemmer and entitled, "Methods and Compositions for Metabolic and Cellular Engineering." The art contains many examples of the use of such techniques. Thus, other publications such as Minshull and Stemmer ((1999) *Current Opinion in Chemical Biology* 3:284-290) and Christians *et al.* ((1999) *Nature Biotechnology* 17: 259-264) demonstrate that experiments comprising shuffling and large-scale functionality assays are now considered routine in the art. Because such experiments are routine, they would not be considered "undue experimentation" under *In re Wands* and *In re Jackson*. Accordingly, Applicants submit that the practice of the claimed methods does not require undue experimentation.

Applicants again note that other cases involving molecular biology also support Applicants' position. The court in *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81 (Fed. Cir. 1986) held that claims were enabled where the necessary method for producing monoclonal antibodies was well known in the art prior to the filing date. Similarly, in the recent case *Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 56 U.S.P.Q.2d 1332 (Fed. Cir. 2000), *reh'g en banc denied* (Nov. 14, 2000), the Federal Circuit found claims to be enabled where steps of the claimed method required the use of molecular biology techniques and a test for functionality. In finding that the claims were enabled, the court noted that "all of the methods needed to practice the invention were well known to those skilled in the art" and that "the process used conventional and well-known genetic engineering techniques." 56 U.S.P.Q.2d at 1337.

The Examiner continues to maintain that Broun *et al.* teaches the unpredictability in the field. Applicants continue to maintain, for the reasons made of record in the Amendment filed on October 23, 2003 and the Amendment After Final filed on March 17, 2003, that Broun *et al.* teaches away from making amino acid substitutions that conserve function of the polypeptide as claimed by the present invention. Moreover, Broun *et al.* used common techniques (similar to those outlined above) to identify the critical residues of the protein and subsequently change

them to destroy the function of the polypeptide. The Broun *et al.* reference therefore provides further evidence that the techniques required to generate the sequences encompassed by the instant claims are routinely used in the art.

Accordingly, in view of the guidance in the specification and the knowledge in the art, claims 2-4 and 25-26 which recite 95% sequence identity to SEQ ID NO: 3 satisfy the enablement requirement under 35 U.S.C. §112, first paragraph.

Similarly, claims 42-46 have been amended to expedite prosecution and now recite a nucleic acid molecule having at least 200 consecutive nucleotides of SEQ ID NO: 3 and encoding a full-length LOX polypeptide having LOX activity. First, the state of the art is such that it would have been routine to make the DNA molecules encompassed by SEQ ID NO: 3 given that SEQ ID NO: 3 was provided in the specification. Moreover, as amended, the genus claimed is significantly smaller than fragments of 200 consecutive nucleotides, and each embodiment can be readily identified in a manner routine in the art, obtained using conventional methods, and assayed for LOX activity without using undue experimentation. Applicants, submit amended claims 42-46 are clearly enabled under 35 U.S.C. §112, first paragraph.

In view of the amendments and above remarks, it is apparent that those of skill in the art would be able to practice the present claims without undue experimentation. Accordingly, the enablement rejection of claims 2-4, 25-36, and 42-46 should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn

Claims 2-4, 25-26, and 32-46 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 37-46 have been canceled. Claims 2, 32, and 42 have been amended. This rejection is respectfully traversed.

The Examiner indicates that term "LOX-like activity" in claim 2 is indefinite. The Examiner asserts that it is unclear whether the polypeptide has LOX activity or not. While Applicants respectfully disagree with the position of the Examiner concerning the term "LOX-

like activity", Applicants have amended claims 2 and 42 to replace this term with "LOX activity". In addition, claim 32 has been amended to independent form and thus, no longer recites the limitations of claim 2, particularly "LOX-like activity". Accordingly, in view of the amendments, claims 2-4, 25-26, 32-36, and 42-46 are not indefinite.

In view of the amendments and remarks, it is submitted that the rejections under 35 U.S.C. § 112, second paragraph, should be withdrawn.

#### CONCLUSIONS

In view of the above amendments and remarks, Applicants submit that the rejections of the claims under 35 U.S.C. § 112 are overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 C.F.R. § 1.136(a), and any fee

Appl. No.: 09/714,767  
Filed: November 16, 2000  
Page 17 of 17

required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



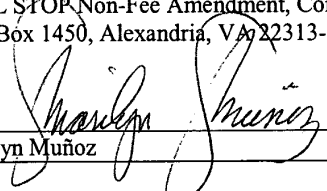
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